

## REMARKS

### I. Amendments

By this amendment, claims 28-49 have been cancelled. New claim 50 has been added. This amendment adds no new matter to the specification. Support for new claim 50 may be found in page 29, lines 26-30 and page 30, lines 2-5 *inter alia*.

No amendment of inventorship is necessitated by this amendment.

### II. Discussion of the Rejection for Obviousness-Type Double Patenting

Claims 1, 4-7, 11 and 22-49 have been rejected under the judicially-created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1-19 of U.S. Patent No. 6,329,403 (Odaka *et al.*). Applicants respectfully traverse the rejection.

As an initial matter, Applicants note that an obviousness-type double patenting rejection was made over U.S. Patent No. 6,329,404 (Ikeda *et al.*) in the Office Action dated June 18, 2003. Applicants are uncertain if that rejection has been overcome, or if the Examiner has made a typographical error on page 7 of the present Office Action, as it includes an obviousness-type double patenting rejection over a new reference, U.S. Patent No. 6,329,403 (Odaka *et al.*), yet includes comments relevant to the previous reference. Applicants wish to point out that their comments on page 19 of the response filed December 18, 2003 were directed to the '404 reference. The Examiner's clarification of this rejection is respectfully requested.

In this regard, Applicants wish to point out that the '404 reference Ikeda *et al.* does not teach or suggest combination with anorectics, as they have previously argued. The '404 reference does not even include a claim 33, a claim 41 or a claim 48, so the Examiner's comments at the bottom of page 7 do not appear to recognize that Applicants' previous arguments were to overcome a reference apparently not now at issue. For this reason Applicants believe that the Examiner has somehow confused the '404 and '403 references.

In the remarks on page 7, the Examiner has stated that "it would be inherent that a method for treating diabetes would include lowering the concentration of glycosylated

hemoglobin, since it is well-known that glycosylated hemoglobin is a measurement of glucose and its concentration would be lowered in a method for treating diabetes.”

However, not all anti-diabetic agents lower the concentration of glycosylated hemoglobin. A supplemental reference, Buchanan *et al.* (Eur. J. Clin. Pharmacol. article, 1988) accompanies this response in attached Appendix A. In this journal article, the well-known anti-diabetic agent acarbose is shown to provide no significant improvement in glycosylated hemoglobin.

Thus Applicants do not believe that there is an obviousness-type double patenting issue with independent claim 1, or independent claims 7 and 25. Claims 4-6, 11, 22-24, 26 and 27 depend upon claim 1. Applicants assert that the more specific dependent claims are also patentable for the reason provided above. Claims 28-49 have been cancelled.

Therefore, Applicants respectfully request clarification and withdrawal of the rejection for obviousness-type double patenting.

### **III. Discussion of the Rejection under 35 U.S.C. Sec. 112, Second Paragraph**

Claims 1, 4-6, 11-24 and 26-49 have been rejected under 35 U.S.C. Sec. 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Applicants respectfully traverse the rejection.

The Examiner apparently has objected to the phrase “in combination with” as being unclear. Yet this same phrase appears in the claims of the parent patent, U.S. Patent No. 6,329,403, which the present Examiner also examined. Applicants do not understand how phraseology previously acceptable is now not acceptable or even unclear to the same Examiner. The rejection thus appears inconsistent with the Examiner’s own practices.

Futhermore, Applicants do not know how the phrase “in combination with” could be made more clear. In claim 1, “an effective amount of an insulin sensitizer in combination with an anorectic” is recited. How could it be unclear whether or not an anorectic is required?

Claims 4-6, 11, 22-24, 26 and 27 depend upon claim 1. Applicants assert that the more specific dependent claims are also patentable for the reason provided above. Claims 28-49 have been cancelled.

Therefore Applicants respectfully request withdrawal of the 35 U.S.C. Sec. 112, second paragraph rejection.

#### **IV. Discussion of the Rejection under 35 U.S.C. Sec. 112, First Paragraph**

Claims 1, 4-6, 11, 22-24 and 26-49 have been rejected under 35 U.S.C. Sec. 112, first paragraph as allegedly lacking enablement. Applicants respectfully traverse the rejection.

Applicants find the Examiner's comments in the first paragraph on page 2 to be confusing, as the Examiner first indicates that there is enablement for insulin sensitizers of formula I, then indicates that there is not enablement for any and all insulin sensitizers. Applicants respectfully wish to point out that independent method claim 1 is already limited to insulin sensitizers of formula (I).

Moreover, dependent claims 5, 6 and 22-24 recite either specific anorectics or classes of anorectics. Surely claims 6 and 24 (which recite specific anorectics) have been mistakenly included in this rejection.

The Examiner therefore is respectfully requested to reconsider the rejection.

By this amendment, Applicants have cancelled claims 28-49, so the Examiner's comments in the second paragraph of page 2 are moot, as the pending claims do not include reference to the treatment of complications of diabetes.

Therefore Applicants respectfully request withdrawal of the 35 U.S.C. Sec. 112, first paragraph rejection.

#### **V. Discussion of the Rejection under 35 U.S.C. Sec. 102(a)**

Claims 28-32, 34-40, 42-47 and 49 have been rejected under 35 U.S.C. Sec. 102(a) as allegedly being anticipated by WO 98/11884. Applicants respectfully traverse the rejection.

By this amendment, Applicants have cancelled claims 28-49, thereby rendering the rejection moot.

Therefore, Applicants respectfully request withdrawal of the 35 U.S.C. Sec. 102(a) rejection.

**VI. Discussion of the Rejection under 35 U.S.C. Sec. 103(a) over WO 98/11884 and Russell *et al.* (Medline AN 97386874) in view of Biosis AN 1997**

Claims 1, 4-6, 11-24 and 26-49 have been rejected under 35 U.S.C. Sec. 103(a) as allegedly being unpatentable over WO 98/11884 and Russell *et al.* (Medline AN 97386874) in view of Biosis AN (1997: 356824). Applicants respectfully traverse the rejection.

Simply because an agent is an anti-diabetic compound, does not mean that it will lower the concentration of glycosylated hemoglobin. The Examiner is requested to refer to the Buchanan *et al.* article of attached Appendix A and the argument made in Sec. II above for support of this statement.

The method recited in claim 1 is limited to certain insulin sensitizers of general formula I. There is no suggestion by the combined teachings of the cited references that the recited insulin sensitizers in combination with anorectics can be used for lowering the concentration of glycosylated hemoglobin. Thus the combined teaching of the cited references does not render the method as set forth in independent claim 1 obvious.

Claims 4-6, 11, 22-24, 26 and 27 depend upon claim 1. Applicants assert that the more specific dependent claims are also patentable for the reason provided above. Claims 28-49 have been cancelled.

Therefore Applicants respectfully request withdrawal of the 35 U.S.C. Sec. 103(a) rejection.

**VII. Discussion of the Rejection under 35 U.S.C. Sec. 103(a) over Medline AN and WO 93/03724 in view of Biosis AN 1997**

Claims 1, 4-6, 11-24 and 26-49 have been rejected under 35 U.S.C. Sec. 103(a) as allegedly being unpatentable over Medline AN (1998: 152487) and WO 93/03724 in view of Biosis AN (1997: 356824). Applicants respectfully traverse the rejection.

Simply because an agent is an anti-diabetic compound, does not mean that it will lower the concentration of glycosylated hemoglobin. The Examiner is requested to refer to the

Buchanan *et al.* article of attached Appendix A and the argument made in Sec. II above for support of this statement.

Applicants disagree with the Examiner's characterization of the WO 93/03724 reference. The "3-guanidinopropionic acid (3-GPA)" in WO 93/03724 is completely different from "an anorectic" of the present invention. This is so because according to WO 93/03724:

- (1) 3-GPA increases endurance, stamina and exercise capacity (page 1 lines 10-12);
- (2) This effect (i.e., the effect of decreasing body weight by 3-GPA) has been attributed to decreased skeletal muscle mass and has not been attributed to reduced adiposity or decreased lipid storage (page 5 lines 1-5);
- (3) in a human patient suffering from a chronic disease, such as cancer, 3-GPA may be useful to prevent cachexia, which is a general wasting of the body during a chronic disease, and increase the survival time of such a patient (page 13 lines 4-8).
- (4) 3-GPA may be dissolved in juices, such as orange juice (page 13 lines 20-21);
- (5) 3-GPA can be used as an additive to powdered food products, including pudding and pie filling mixes (page 13 lines 28-29);
- (6) 3-GPA can be used in prepared foods themselves; for example, it can be used as an additive in cakes, pasta products, candy, cookies (page 13 lines 32-34).

Thus, 3-GPA has its unique mechanism of decreasing skeletal muscle mass, and this mechanism is quite different from that of an anorectic employed in the present invention, namely a mechanism of suppressing appetite.

Those skilled in the art would not think of substituting "3-GPA", which is used in a cancer patient for the purpose of increasing its survival time, and used in orange juice, pudding, cakes, pasta products, candy, cookies and the like for the purpose of increasing endurance, stamina and exercise capacity, with "an anorectic" of the present invention which is used for the purpose of suppressing appetite.

Furthermore, WO 93/03724 nowhere discloses or suggests "a method for lowering the concentration of glycosylated hemoglobin".

The method recited in claim 1 is limited to certain insulin sensitizers of general formula I. There is no suggestion by the combined teachings of the cited references that the recited insulin sensitizers in combination with anorectics can be used for lowering the concentration of

glycosylated hemoglobin. Thus the combined teaching of the cited references does not render the method as set forth in independent claim 1 obvious.

Claims 4-6, 11, 22-24, 26 and 27 depend upon claim 1. Applicants assert that the more specific dependent claims are also patentable for the reason provided above. Claims 28-49 have been cancelled.

Therefore Applicants respectfully request withdrawal of the 35 U.S.C. Sec. 103(a) rejection.

### VIII. Conclusion

Reconsideration of the claims and allowance is requested.

Should the Examiner believe that a conference with Applicants' attorney would advance prosecution of this application, she is respectfully requested to call Applicants' attorney at (847) 383-3391.

Respectfully submitted,

Dated: September 8, 2005

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